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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/575,438

04/11/2006

Christopher Wheeler

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50670 7590 10/18/2007
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EXAMINER

GODDARD, LAURA B

ART UNIT

PAPER NUMBER

1642

MAIL DATE

DELIVERY MODE

10/18/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/575,438

Applicant(s)

WHEELER ET AL.

Examiner

Laura B. Goddard, Ph.D.

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1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 4, 15 and 21-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-14 and 16-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 April 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>4/30/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The Election filed August 13, 2007 in response to the Office Action of July 11, 2007 is acknowledged and has been entered. Applicants elected without traverse Group I, the species of chemotherapeutic "temolozomide," and the species of dendritic cell "primed".

Claims 1-24 are pending. Claims 21-24 are withdrawn from further consideration by the examiner under 35 CFR 1.142(b) as being drawn to non-elected inventions. Claims 4 and 15 are withdrawn as being drawn to non-elected species. Claims 1-3, 5-14 and 16-20 are currently under prosecution.

Specification

2. The disclosure is objected to because of the following informalities: There appears to be incongruent statements on page 5, lines 5-9 ([10]) in reference to Figure 2. The specification states: "Survival of the vaccine + chemotherapy group was significantly greater relative to *both* survival in the other two groups, and greater than survival in the chemotherapy group alone". However, the specification subsequently states: "Survival of the vaccine group tended to be lower but was not statistically different than that of the vaccine + chemotherapy group". It is unclear how the survival of the vaccine + chemotherapy group can be significantly greater than *both* other groups (which includes the vaccine group) at the same time the vaccine group is not statistically different from the vaccine + chemotherapy group. It appears the specification intends to state in lines 5-6 that the survival of the vaccine + chemotherapy group is significantly

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greater relative to the *combined survival values* of the other two groups (vaccine group and chemotherapy group). Clarification is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 3 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "wherein said DC are autologous tumor antigen-presented DC". It is unclear if the adjective "autologous" is intended to describe the tumor antigen, the DC itself, or both. Clarification is required. For examination purposes, Examiner interprets the claim to mean the DC are autologous.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

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only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1, 5, 6, 12, 16, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Tong et al (Cancer Research, 2001, 61:7530-7535).

The claims are drawn to a method for treating a disease condition in a mammal, comprising: administering at least one vaccination of dendritic cells (DC) to said mammal; and administering a regimen of chemotherapy to said mammal (claim 1), wherein administering said at least one vaccination further comprises administering at least three vaccinations of DC (claim 5), wherein each of said at least one vaccination comprises from about 10^5 to about 10^7 DC (claim 6), a method of increasing chemosensitivity of a mammal comprising: providing at least one vaccination of DC; and administering said at least one vaccination of DC to said mammal (claim 12), wherein administering said at least one vaccination further comprises administering at least three vaccinations of DC (claim 16), wherein each of said at least one vaccination comprises from about 10^5 to about 10^7 DC (claim 17).

It is noted the specification discloses that a "disease condition" includes cancer (p. 7, [23]).

Tong et al teach a method for treating cancer in a mammal (mouse) comprising administering four separate injections of DC with each injection at an amount of 10^6 DC, subsequent to three treatments of chemotherapy (abstract; p. 7531, col. 1). Tong et al teach that the combination of chemotherapy with DC treatment markedly enhanced survival of mice with tumors as compared to mice treated with chemotherapy or DC alone (p. 7531 col. 2 through p. 7532, col. 2; Figures 1C, 2C, 3). Administration of DC

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and chemotherapy resulted in enhanced suppression or complete suppression of tumor growth compared to mice treated with either DC or chemotherapy alone (p. 7531 col. 2 through p. 7532, col. 2; Figures 1A, B and 2A, B). Although Tong et al does not specifically state the method increases chemosensitivity of a mammal, the method taught by the prior art comprises the same method steps of providing at least one vaccination of DC and administering said at least one vaccination of DC to said mammal as recited in the claimed method, hence the method taught by the prior art would increase chemosensitivity of a mammal.

5. Claims 12-14, 16, 17, 19 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Yu et al I (Cancer Research, 2001, 61:842-847, IDS).

The claims are drawn to a method of increasing chemosensitivity of a mammal comprising: providing at least one vaccination of DC; and administering said at least one vaccination of DC to said mammal (claim 12), wherein said DC are primed *ex vivo* (claim 13), wherein said DC are autologous tumor antigen-presented DC (claim 14), wherein administering said at least one vaccination further comprises administering at least three vaccinations of DC (claim 16), wherein each of said at least one vaccination comprises from about 10^5 to about 10^7 DC (claim 17), whereby chemosensitivity of said mammal is increased with respect to chemotherapeutic treatment of a cancer of the central nervous system or glioblastoma multiforme (claims 19 and 20).

Yu et al I teach a method of treating glioblastoma multiforme comprising administering three vaccinations of 10^6 DC to patients (mammalian), wherein the DC are autologous and primed *ex vivo* (abstract; p. 842, both columns; p. 843, col. 1 last paragraph bridging to col. 2). Although the reference does not specifically teach that the chemosensitivity of the patient is increased or increased with respect to chemotherapeutic treatment of glioblastoma multiforme, the method taught by the prior art comprises the same method steps of providing at least one vaccination of DC and administering said at least one vaccination of DC to said mammal as recited in the claimed method, hence the method taught by the prior art would increase chemosensitivity of a mammal and increase chemosensitivity with respect to chemotherapeutic treatment of glioblastoma multiforme.

6. Claims 1-3, 8, 10-14, 19, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent Application Publication 2002/0119121, Vitiello et al, filed 9/6/2001, published 8/29/2002.

The claims are drawn to a method for treating a disease condition in a mammal, comprising: administering at least one vaccination of dendritic cells (DC) to said mammal; and administering a regimen of chemotherapy to said mammal (claim 1), wherein said DC are primed *ex vivo* (claim 2), wherein said DC are autologous tumor antigen-presented DC (claim 3), wherein said administering of said at least one vaccination of DC occurs prior to administering said regimen of chemotherapy to said

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mammal (claim 8), wherein said disease condition is a cancer of the central nervous system and is glioblastoma multiforme (claims 10 and 11); a method of increasing chemosensitivity of a mammal comprising: providing at least one vaccination of DC; and administering said at least one vaccination of DC to said mammal (claim 12), wherein said DC are primed *ex vivo* (claim 13), wherein said DC are autologous tumor antigen-presented DC (claim 14), whereby chemosensitivity of said mammal is increased with respect to chemotherapeutic treatment of a cancer of the central nervous system or glioblastoma multiforme (claims 19 and 20).

Vitiello et al teach a method of treating cancer in a patient (mammalian) comprising administering DC to a patient prior to, during, or subsequent to chemotherapy treatment ([2]; [83]; [135]; [140]), wherein the DC are autologous and primed *ex vivo* with tumor antigens from the patient ([36]; [59]; [65-72]; [79-83]; [96]; [99]; [102-103]; [114]), wherein the cancer is glioblastoma multiforme ([51]; Table 1). Although the reference does not specifically teach that the chemosensitivity of the patient is increased or increased with respect to chemotherapeutic treatment of glioblastoma multiforme, the method taught by the prior art comprises the same method steps of providing at least one vaccination of DC and administering said at least one vaccination of DC to said mammal as recited in the claimed method, hence the method taught by the prior art would increase chemosensitivity of a mammal and increase chemosensitivity with respect to chemotherapeutic treatment of glioblastoma multiforme.

7. Claims 1-3, 5, 6, 7, 10-14, 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent Application Publication 2004/0057935, Yu et al II, filed 9/20/2002, published 3/25/2004.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The claims are drawn to a method for treating a disease condition in a mammal, comprising: administering at least one vaccination of dendritic cells (DC) to said mammal; and administering a regimen of chemotherapy to said mammal (claim 1), wherein said DC are primed *ex vivo* (claim 2), wherein said DC are autologous tumor antigen-presented DC (claim 3), wherein administering said at least one vaccination further comprises administering at least three vaccinations of DC (claim 5), wherein each of said at least one vaccination comprises from about 10^5 to about 10^7 DC (claim 6), wherein each of said at least one vaccination of DC comprises about 10×10^6 to about 40×10^6 DC (claim 7), wherein said disease condition is a cancer of the central nervous system and is glioblastoma multiforme (claims 10 and 11); a method of increasing chemosensitivity of a mammal comprising: providing at least one vaccination of DC; and administering said at least one vaccination of DC to said mammal (claim 12), wherein said DC are primed *ex vivo* (claim 13), wherein said DC are autologous tumor

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antigen-presented DC (claim 14), wherein administering said at least one vaccination further comprises administering at least three vaccinations of DC (claim 16), wherein each of said at least one vaccination comprises from about 10^5 to about 10^7 DC (claim 17), wherein each of said at least one vaccination of DC comprises about 10×10^6 to about 40×10^6 DC (claim 18), whereby chemosensitivity of said mammal is increased with respect to chemotherapeutic treatment of a cancer of the central nervous system or glioblastoma multiforme (claims 19 and 20).

Yu et al II teach a method of treating cancer comprising administering DC to a patient (mammalian) ([2-12]; [15-19]; [24-25]; Examples 1-9), wherein the DC can be autologous and primed *ex vivo* with a tumor antigen before administration to the patient ([9-10]; [27]), wherein the patient can receive from one to about five administrations of 10^6 DC, wherein the patient can be administered with about 10^5 to about 10^7 DC, which would include doses in the range of about 10×10^6 to about 40×10^6 DC ([33]), wherein the method further comprises administering chemotherapy either prior to or simultaneously with DC ([34]), and wherein the cancer is of the central nervous system or is glioblastoma multiforme ([3]; [25]; Examples 1-6). Although the reference does not specifically teach that the chemosensitivity of the patient is increased or increased with respect to chemotherapeutic treatment of glioblastoma multiforme, the method taught by the prior art comprises the same method steps of providing at least one vaccination of DC and administering said at least one vaccination of DC to said mammal as recited in the claimed method, hence the method taught by the prior art would increase

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chemosensitivity of a mammal and increase chemosensitivity with respect to chemotherapeutic treatment of glioblastoma multiforme.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being obvious over US Patent Application Publication 2004/0057935, Yu et al II, filed 9/20/2002, published 3/25/2004, in view of Friedman et al (Clinical Cancer Research, 2000, 6:2585-2597).

The applied reference has a common inventor with the instant application.

Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the

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application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The claims are drawn to a method for treating a disease condition in a mammal, comprising: administering at least one vaccination of dendritic cells (DC) to said mammal; and administering a regimen of chemotherapy to said mammal (claim 1), wherein said regimen of chemotherapy includes the administration of temolozomide (claim 9).

It is noted the specification discloses that a "disease condition" includes cancer (p. 7, [23]).

Yu et al II teach a method of treating glioblastoma multiforme comprising administering DC to a patient (mammalian) wherein the method further comprises administering chemotherapy as set forth above.

Yu et al II does not teach that the chemotherapy is temozolomide.

Friedman et al teach successful treatment of glioblastoma multiforme in patients comprising administering temozolomide (abstract; Table 4; p. 2592, col. 1; Fig. 2). Friedman et al teach that combining two or more drugs that have different cytotoxic mechanisms or are subject to different mechanisms of resistance can produce synergistic effects. Temozolomide can be coadministered with various agents (p. 2593, col. 1; p. 2594, col. 1, last para).

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It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use temozolomide as the chemotherapeutic in the method taught by Yu et al II because Friedman et al teach using temozolomide to treat glioblastoma multiforme. One would have been motivated to use temozolomide as the chemotherapeutic in the method taught by Yu et al II because Friedman et al demonstrate that temolozomide successfully and safely treats glioblastoma multiforme and expressly suggests combining temolozomide with other agents that use different cytotoxic mechanisms to produce synergistic effects. One of ordinary skill in the art would have a reasonable expectation of success treating glioblastoma multiforme with DC and temolozomide because both agents are known to treat glioblastoma multiforme.

9. Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Application Publication 2002/0119121, Vitiello et al, filed 9/6/2001, published 8/29/2002, in view of Friedman et al (Clinical Cancer Research, 2000, 6:2585-2597).

The claims are drawn to a method for treating a disease condition in a mammal, comprising: administering at least one vaccination of dendritic cells (DC) to said mammal; and administering a regimen of chemotherapy to said mammal (claim 1), wherein said regimen of chemotherapy includes the administration of temolozomide (claim 9).

It is noted the specification discloses that a "disease condition" includes cancer (p. 7, [23]).

Vitiello et al teach a method of treating glioblastoma multiforme comprising administering DC to a patient (mammalian) wherein the method further comprises administering chemotherapy as set forth above.

Vitiello et al does not teach that the chemotherapy is temozolomide.

Friedman et al teach successful treatment of glioblastoma multiforme in patients comprising administering temozolomide (abstract; Table 4; p. 2592, col. 1; Fig. 2).

Friedman et al teach that combining two or more drugs that have different cytotoxic mechanisms or are subject to different mechanisms of resistance can produce synergistic effects. Temozolomide can be coadministered with various agents (p. 2593, col. 1; p. 2594, col. 1, last para).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use temozolomide as the chemotherapeutic in the method taught by Vitiello et al because Friedman et al teach using temozolomide to treat glioblastoma multiforme. One would have been motivated to use temozolomide as the chemotherapeutic in the method taught by Vitiello et al because Friedman et al demonstrate that temolozomide successfully and safely treats glioblastoma multiforme and expressly suggests combining temolozomide with other agents that use different cytotoxic mechanisms to produce synergistic effects. One of ordinary skill in the art would have a reasonable expectation of success treating glioblastoma multiforme with DC and temolozomide because both agents are known to treat glioblastoma multiforme.

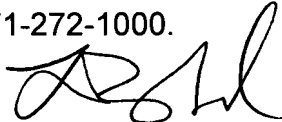
10. **Conclusion:** No claim is allowed.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Laura B Goddard, Ph.D.
Examiner
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